

## CLAIMS

1. A conformational antibody capable of specifically binding to the natural HCV viral envelope.
2. A conformational antibody according to claim 1, capable of specifically binding to the natural HCV E2 protein.
3. A conformational antibody according to claim 1 or 2, capable of neutralizing HCV infections in patients.
4. A conformational antibody according to any of claims 1 to 3, capable of precipitating the HCV E1E2 complex under its covalent or non covalent forms.
5. A conformational antibody according to any of claims 1 to 4, capable of specifically binding to the natural HCV E1 protein.
6. A conformational antibody according to any of claims 1 to 5, capable of specifically binding to the natural HCV E1 protein, to the natural HCV E2 protein, and of precipitating the HCV E1E2 complex under its covalent or non covalent forms.
7. A conformational antibody according to any of claims 1 to 6, capable of specifically binding an epitope constituted of at least one of the following sequences:
  - amino acids 297 to 306 of HCV protein E1 (SEQ ID NO: 1);
  - amino acids 480 to 494 of HCV protein E2 (SEQ ID NO: 2);
  - amino acids 613 to 621 of HCV protein E2 (SEQ ID NO: 3).
8. A conformational antibody according to claim 7, capable of specifically binding to an epitope constituted of each of the following sequences:
  - amino acids 297 to 306 of HCV protein E1 (SEQ ID NO: 1);
  - amino acids 480 to 494 of HCV protein E2 (SEQ ID NO: 2);
  - amino acids 613 to 621 of HCV protein E2 (SEQ ID NO: 3).

9. A conformational antibody according to any of claims 1 to 8, wherein said antibody is a monoclonal antibody.
10. A monoclonal antibody according to any of claims 1 to 9, secreted by the hybridoma deposited at the CNCM (Collection Nationale de Culture de Microorganismes, Institut Pasteur, Paris, France) on March 19, 2003, under accession number CNCM I-2983.
11. A monoclonal antibody according to any of claims 1 to 9, secreted by the hybridoma deposited at the CNCM (Collection Nationale de Culture de Microorganismes, Institut Pasteur, Paris, France) on March 19, 2003, under accession number CNCM I-2982.
12. A hybridoma deposited at the CNCM (Collection Nationale de Culture de Microorganismes, Institut Pasteur, Paris, France) on March 19, 2003, under accession number CNCM I-2983.
13. A hybridoma deposited at the CNCM (Collection Nationale de Culture de Microorganismes, Institut Pasteur, Paris, France) on March 19, 2003, under accession number CNCM I-2982.
14. A pharmaceutical composition comprising as active substance at least one of the antibodies of claims 1 to 11 and a pharmaceutically acceptable vehicle.
15. Use of at least one of the antibodies of claims 1 to 11, for the preparation of a medicament for the diagnostic, the prevention or the treatment of HCV infections.
16. An enveloped viral particle capable of binding to at least one of the antibodies of claim 10 or 11.
17. An antibody which binds to the enveloped viral particle of claim 16.
18. A composition of HCV viral particles derived from initial samples of human blood, plasma or sera, wherein the concentration of HCV RNA copies is about 100 to 1000 fold higher than the concentration of HCV RNA copies in the initial samples of

human, blood, plasma or sera from which it is derived, and is in particular higher than about  $10^7$  copies/ml.

19. A composition according to claim 18, wherein the number of HCV RNA copies is from about  $10^8$  to about  $10^9$  UI per mg of protein.
20. A composition according to claim 18 or 19, wherein the volume of said composition is from about 0.1 ml to about 10 ml.
21. An isolated HCV enveloped subviral particle substantially devoid of HCV RNA and of HCV core protein.
22. An isolated HCV enveloped subviral particle according to claim 21, wherein said subviral particle is liable to bind to any of the antibodies of claims 1 to 11.
23. A composition comprising purified HCV enveloped complete viral particles, said purified HCV enveloped complete viral particles containing HCV RNA, HCV core protein and HCV envelope, and being liable to bind to any of the antibodies of claims 1 to 11.
24. A process for preparing a composition of HCV viral particles comprising the following steps:
  - at least two ultracentrifugations of a sample resulting from a clarified plasmapheresis of a HCV infected patient to obtain a HCV enriched pellet;
  - resuspension of the HCV enriched pellet in an aqueous solution to obtain a composition of HCV viral particles.
25. A composition of HCV viral particles such as obtained according to the process of claim 24.
26. A process for preparing a composition of HCV enveloped subviral particles comprising the following steps :
  - at least two ultracentrifugations of a sample resulting from a clarified plasmapheresis of a HCV infected patient to obtain a HCV enriched pellet;

- resuspension of the HCV enriched pellet in an aqueous solution;
- ultracentrifugation of the resuspended HCV enriched pellet in a sucrose density gradient to separate the elements of the resuspended HCV enriched pellet into fractions according to their density;
- recovery of the fractions containing substantially no HCV RNA, substantially no HCV core protein and containing particles capable of binding to the monoclonal antibody of claim 10 or 11, in particular fractions with a sucrose density of approximately 1.13 to 1.15 g/ml, to obtain a composition of HCV enveloped subviral particles.

27. A composition of HCV enveloped subviral particles such as obtained according to the process of claim 26.

28. A process for preparing a composition of purified HCV enveloped complete viral particles comprising the following steps :

- at least two ultracentrifugations of a sample resulting from a clarified plasmapheresis of a HCV infected patient to obtain a HCV enriched pellet;
- resuspension of the HCV enriched pellet in an aqueous solution;
- ultracentrifugation of the resuspended HCV enriched pellet in a sucrose density gradient to separate the elements of the resuspended HCV enriched pellet into fractions according to their density;
- recovery of the fractions containing from about  $5 \cdot 10^5$  to about  $10^6$  UI of HCV RNA per ml, from about 50 to about 100 pg of HCV core protein per ml, and containing particles capable of binding to the monoclonal antibody of claim 10 or 11, in particular fractions with a sucrose density of approximately 1.17 to 1.21 g/ml, to obtain a composition of purified HCV enveloped complete viral particles.

29. A composition of purified HCV enveloped complete viral particles such as obtained according to the process of claim 28.

30. A process for preparing a monoclonal antibody of claim 10, comprising the following steps:

- immunizing an animal, in particular a mammal, with a composition of HCV viral particles according to claim 18, or such as prepared according to claim 24, and recovering the generated antibodies;
- selecting, among the generated antibodies, monoclonal antibodies on their ability of binding to the HCV viral particles contained in the above mentioned composition of HCV viral particles.

31. A process for preparing a monoclonal antibody of claim 11, comprising the following steps:

- immunizing an animal, in particular a mammal, with a composition of purified HCV enveloped complete viral particles according to claim 23, or such as prepared according to claim 28, and recovering the generated antibodies;
- selecting, among the generated antibodies, monoclonal antibodies on their ability of binding to the purified HCV enveloped complete viral particles contained in the above mentioned composition of purified HCV enveloped complete viral particles.

32. A pharmaceutical composition comprising as active substance the subviral particles of claim 21 or 22, or the composition of claim 27, and a pharmaceutically acceptable vehicle.

33. Use of the HCV enveloped subviral particles of claim 21 or 22, or of the composition of claim 27, to induce an immune reaction against said HCV enveloped subviral particles or against HCV enveloped complete viral particles as defined in claim 22.

34. Use of the HCV enveloped subviral particles of claim 21 or 22, or of the composition of claim 27, for the preparation of a medicament for the diagnostic, the prevention or the treatment of HCV infections.